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09/582,809

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EXAMINER

MYERS, CARLA J

ART UNIT

PAPER NUMBER

1634

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/582,809

Applicant(s)

SEIDEL ET AL.

Examiner

Carla Myers

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/18/07.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 186-197, 199-203, 205-208 and 210-220 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 186-197, 199-203, 205-208 and 210-220 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 7/18/07.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 18, 2007 has been entered.

2. Applicant's arguments and amendments set forth in the response of July 18, 2007 have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. The following Office action contains new grounds of rejection and is made non-final.

3. Claims 186-197, 199-203, 205-208 and 210-220 are newly added and have been examined herein.

Claim Objections

4. Claims 186-197, 199-203, 205-208 and 210-220 are objected to because of the following informalities: The claims recite "at least 1200 sorts second," whereas the claims should read, for example, "at least 1200 sorts **per** second."

Appropriate correction is required.

Claim Rejections - 35 USC § 112 second paragraph

5. Claims 186-197, 199-203, 205-208, 210-220 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 217- 220 indefinite over the recitation of "low number of said sperm cells relative to a typical artificial insemination sample." The term "low" is a relative term which renders the claim indefinite. The phrase "low number" is not clearly defined by the claim and the specification does not provide a standard for ascertaining the requisite number of sperm which would be considered low for any mammal. While the specification does not define the phrase "low number," the specification (page 19) states that a "low dose" is less than one-half or preferably less than about 10% of the typical number of sperm provided in a "typical artificial insemination event." However, the specification does not clearly set forth what is intended to constitute a typical artificial insemination event. The specification also states that with respect to bovine, a low dose may be 500,000 sperm or 300,000 sperm or lower. For equine, it is stated that a low dose may be 25, 10, 5 or even one million sperm. Clearly, there is a significant degree of variability surrounding what might constitute "low number" (e.g., 25 million versus 1 million) and there is no specific teaching in the specification or art as to what is generally accepted by practitioners as a "low number" with respect to bovine, equine and other members of the broadly claimed genus of nonhuman mammals. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

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Further, the claims have been amended to recite that the step of establishing an artificial insemination sample comprises establishing an artificial insemination sample having a low number of sperm cells relative to a typical artificial insemination sample "selected from the group consisting of..." or "less than about one-half" or "less than about 10 percent" of sperm cells in a typical artificial insemination sample. It is unclear as to whether the artificial insemination sample has the stated number of sperm cells (i.e., the one-half, the 10% or the 100,000 bovine cells or one million equine cells etc), or if the low number of sperm are relative to the stated number of sperm. In the later case, it is unclear as to whether the claims intend to compare the number of sperm of any mammal to the number of sperm of a bovine or equine, or if the artificial insemination sample is intended to be limited to one that comprises bovine sperm (claim 219) or equine sperm (claim 220).

Response to arguments:

In the response, Applicants state that the term "low" appears in the title of an article in Exhibit A and is used in the text of articles by Buchanan, Cran, Lindsey, Martinez, Maxwell, Rath, Rigby, Seidel, Vazquez, Hollinshead and Bodmer. Applicants conclude that the term thereby has a known meaning across multiple kinds of animal species. This argument is not persuasive. The rejection was not made on the premise that the term had never before been used in the art. The rejection is based on the finding that there is no art recognized definition for this term. As established by the cited references and the teachings of the specification cited above, the meaning of "low" varies substantially and there is no guidance provided in the specification as to how to

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determine which definition of "low" is intended to be encompassed by the claims.

Further, the cited references are limited to teachings regarding a very limited number of mammalian species, whereas the present claims include any non-human mammalian species. However, the specification and response do not establish that a fixed and clear meaning for "low number of sperm" was known in the art for a representative number of the widely diverse mammalian species encompassed by the claims.

B. Claim 195 is indefinite over the recitation of "after the time which is generally regarded as optimal for a single artificial insemination." This phrase is not clearly defined in the specification and there is no fixed art-recognized definition for this phrase.

Response to arguments:

In the response, Applicants state that the concept of the time regarded as optimal for artificial insemination is known in the field and discussed in the references of Pursley, Nebel, Maatje, Dransfield, Dalton and Rozeboom. This argument is not persuasive. While the cited documents provide examples of the optimal time of artificial insemination in cattle and swine, the cited references do not provide a clear definition for this phrase, particularly as the phrase relates to any non-human mammalian species.

C. Claims 199-204 and 208 are indefinite over the recitation of "establishing a cell source which supplies sperm cells to be sorted" because it is unclear as to what is intended to be encompassed by this step. The claims previously require collecting sperm cells. However, the claims do not clarify how the previously recited steps are

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related to or distinct from the step of establishing a cell source which supplies sperm cells.

Response to arguments:

In the response, Applicants state that the term cell source is illustrated as element (1) in Figure 1 of a flow cytometer and that a cell source is described on page 9 of WO 99/33956. However, while the present specification (which is a 371 of the PCT/US98/27909) uses the term cell source, the specification does not define what is intended to be meant by "establishing a cell source which supplies sperm cells to be sorted"

D. Claims 199-204 are indefinite over the recitation of "sensing a property of said sperm cells" because it is unclear as to what is intended to be encompassed by this phrase. It is unclear as to whether sensing encompasses actually determining a sex characteristic or whether the claims allow for guessing, estimating, inferring or predicting a sex characteristic or some other property based on some undefined attribute or characteristic. The term "sensing" does not clearly describe any particular process step for ascertaining a property of sperm and thereby one of skill in the art cannot determine what is intended to be encompassed by such a step.

Response to arguments:

In the response, Applicants state that the specification of WO 99/33956 describes a cell sensing system and references U.S. Patent 5,135,759. Applicants conclude that one would have access to the WO document and thereby would know what the phrase means. This argument is not persuasive because the claims are not

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limited to the particular cell sensing system that is described on page 9 of WO 99/33956. Further, the specification does not define the phrase "sensing a property of sperm cells" in terms of being limited to the particular embodiment discussed in the cited text at page 9 of the WO 99/33956 document. Thereby, it is maintained that the phrase has not been clearly defined in the specification and there is no art recognized definition for this phrase. An example of what might be encompassed by a phrase is not equivalent to providing a definition for a phrase.

New grounds of rejection:

Claims 186-197, 199-203, 205-208 and 210-220 are indefinite over the recitation of "female of said nonhuman mammal species" because this phrase lacks proper antecedent basis. While the claims previously refer to a male of a non-human mammal species, the claims do not previously refer more generally to a non-human mammal species.

Claims 186-197, 199-203, 205-208 and 210-220 are indefinite over the recitation in (g) of claim 186 of inserting at least a portion of "said artificial insemination sample." The claims previously refer to an artificial insemination obtained in step d, a frozen artificial insemination sample of step e, and a frozen and then thawed artificial insemination sample of step f. It is therefore unclear as to whether the artificial insemination sample referred to in step g is the artificial insemination sample obtained in steps d, e or f, or in each of or any one of steps d, e and f.

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New grounds of rejection:

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(a) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 186-189, 191-197, 202, 208, and 213-219 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (Journal of Animal Science. July 1996, 71 (supplement 1) abstract 513 "Insemination of heifers with very low numbers of frozen spermatozoa"; cited in the IDS) in view of Seidel (Theriogenology. January 1996. vol. 45, page 309; cited in the IDS) and Rens (U.S. Patent No. 5,985,216).

Seidel (July 1996) teaches methods comprising collecting semen from a male bovine, extending the semen in homogenized milk with 7% glycerol extender plus 5% homologous seminal plasma to obtain an artificial insemination sample containing 2 or 5×10^5 total sperm per 0.25ml straw, freezing the artificial insemination sample, thawing the sample to ambient temperature, inseminating synchronized female heifers by inserting half of the semen sample deep into the uterine horns and fertilizing at least

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one egg within said bovine. Seidel teaches that the method using 5×10^5 total frozen/thawed sperm (i.e., a "low number" of sperm) achieved fertilization success rates "statistically comparable" to that obtained using a typical insemination dosage (i.e., 10×10^6 total sperm/inseminate).

Seidel (July 1996) does not teach sorting the sperm prior to artificial insemination.

However, Seidel (Jan 1996) teaches methods for making bovine mammals comprising sorting sperm cells according to sex using flow cytometry wherein the sperm cells are sorted to purity rates of about 90%, establishing an insemination sample, inserting a low dosage ($1-2 \times 10^5$ in .1 ml) of sorted sperm cells into the uterine horns of the female bovine after the onset of estrus; and fertilizing the eggs of the bovine so as to produce at least one offspring of the desired sex. Seidel teaches that 11 of 22 females inseminated with sperm cooled to 5C during shipping were pregnant at 8 weeks. The sperm were deposited deep in the uterine horn ipsilateral to the ovary with the largest follicle being determined by ultrasound.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (July 1996) so as to have sex sorted the sperm as taught by Seidel (Jan 1996) prior to artificial insemination in order to have provided an effective means for controlling the sex of the bovine offspring.

Further, Seidel (July 1996) and Seidel (Jan 1996) do not teach sorting sperm at rates of 1200 sorts/second.

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However, Rens teaches a method of sex-sorting sperm using high speed flow cytometry. In the method of Rens (see columns 4-6), a sample of sperm is obtained from a male mammal, the sperm is stained with Hoechst 33342 dye in order to distinguish between viable and nonviable sperm (column 5, lines 4-10), the sperm are sorted in a high speed flow cytometer using a nozzle that forms a stable droplet containing each individual sperm cell (column 2, lines 23-32), the sperm are sorted according to their sex characteristics and isolated populations of X- and Y-chromosome bearing sperm are collected. Importantly, Rens (col. 5) discloses modifying the MoFlo® high speed cell sorter to include a new elliptical nozzle capable of more accurately orienting sperm for accurate sorting. Rens teaches use of the modified MoFlo® sorter using sampling rates of 500 sperm/second and 2000 sperm/second (column 6). Further, Rens teaches that the modified MoFlo® sorter also allowed for sample rates up to at least 15,000 sperm/sec (column 4, lines 29-31). Rens (col. 2) teaches that the flow cytometry apparatus disclosed therein provides for improved accuracy and efficiency of sorting, as compared to prior art flow cytometers. Rens (col. 2) also discloses the motivation to use high speed cell sorters to maximize the number of sorted sperm per unit time. For example, Rens (col. 4) discuss the requirement to use large quantities of sperm for artificial insemination and states that by using the high speed cell sorter equipped with the nozzle disclosed therein, the yield of sex sorted sperm cells can be increased at least 10 fold, making artificial insemination with sexed semen a more feasible option. Rens (col. 7) also exemplifies a method wherein a total of 50 million X

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and Y sperm were sorted in a 7 hour period using the modified MoFlo® sorter equipped with the new elliptical nozzle.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to have used high sorting rates, including sorting rates of about 1200 sperm/second, in order to have allowed for the faster sorting of sperm so as to have provided adequate quantities of sex-sorted samples that could be used for the insemination process. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

Further, It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." *In re Boesch*, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also *Merck & Co. v. Biocraft Labs. Inc.*, 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious). In the present situation, the prior art teaches provides the motivation to increase sort speeds to at least 1200 sperm/sec and the means for achieving this result (i.e., the modified MoFlo® high speed sorter including the elliptical nozzle of Rens). Thereby, modification of the method of Seidel to use the high speed sorter of Rens to sex-sort sperm cells at rates of 1200 sorts/sec would have been obvious to one of ordinary skill in the art and well within the skill of the art at the time the invention was made.

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Regarding claim 187, Seidel (July 1996) teaches applying the method to bovine.

Regarding claim 188, Seidel (July 1996) teaches that the method is performed under field conditions.

Regarding claim 189, Seidel (July 1996) does not specifically teach repeating the process in a "significant number" of females in a farm or ranch condition. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have repeated the method of Seidel with additional female bovine in "farm or ranch conditions" in order to provide an effective means for inseminating female bovine under natural conditions to produce a large number of bovine offspring.

Regarding claims 191-194, Seidel (July 1996) teaches inserting the semen deep into each uterine horn using an embryo transfer gun (i.e., "embryo transfer equipment").

Regarding claim 195, Seidel (July 1996) teaches performing the artificial insemination procedure 12 hours after the onset of estrous.

Regarding claims 196 and 197, Seidel (July 1996) does not teach using the artificial insemination sample within 17 or 10 hours of establishing the sample. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the artificial insemination sample as soon as possible following the formation of the sample in order to have ensured the viability of the sample, thereby improving the overall effectiveness of the insemination procedure.

Regarding claim 202 and 213-216, Seidel (July 1996) does not specifically teach sorting the sperm into a collector having a cushion to protect the cells from impact with the collector. However, Seidel (Jan 1996) teaches sorting the cells into an extender

containing homologous seminal plasma. Collection into such a medium would have cushioned the sperm cells from impact with the collector. Accordingly, modification of the method of Seidel (July 1996) so as to have sorted the sperm cells using the method of Seidel (Jan 1996) would have resulted in a method that provided the benefit of collecting the sperm cells into a container while cushioning the sperm cells from impact with the collector.

Regarding claim 208, Seidel (July 1996) does not teach staining the cells with a solution of 38uM stain and then concentrating the sperm. However, Rens (col. 5) teaches staining the sperm with 7.1 uM Hoechst 3342 dye per 15×10^6 sperm for 40 min at 32C, sorting the sperm cells and then concentrating the sperm cells. It is noted that the present claims do not specify the type of stain, the final concentration of stain, the number of sperm or the conditions for staining the sperm. However, at the time the invention was made the parameters which effect staining of sperm cells prior to sorting were well known in the art. Thereby, to have determined the optimum concentration of stain, depending on the quantity of sperm and the conditions (time, temp) of staining would have been obvious to one of ordinary skill in the art and well within the skill of the art. As discussed in MPEP 2144.05(b), "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)." Accordingly, it would have

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been obvious to one of ordinary skill in the art and well within the skill of the art to have selected the optimum concentration of stain depending on the concentration of sperm, and the conditions of staining, including to have selected the concentration of 38 μM content of stain, in order to have provided the most effective means for staining the sperm to allow for accurate sorting, while maintaining the integrity and viability of the sperm. Further, with respect to claim 216, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have established a collection container having stream matched physical characteristics in order to have provided the benefit of preserving the integrity of the sperm cells.

Regarding claims 214, the combined references do not specify the size of the collection container. However, it would have been well within the skill of the art at the time the invention was made to have selected a collection container of an appropriate width in order to have prevented damaging the sperm since Rens teaches the criticality of the dimensions of the sorting device and the orientation of the sperm within the sorting device in order to maintain sperm viability (see, for example, column 3).

Regarding claim 217-219, Seidel teaches using 2 or 5×10^5 total sperm. This is considered to be about one half or less than about 10% of sperm cells are used for insemination relative to an unstated amount of a "typical insemination sample."

7. Claims 190 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996) and Rens, as applied above, and further in view of Seidel (1995; cited in the IDS).

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The teachings of Seidel (July 1996), Seidel (Jan 1996) and Rens are presented above. In particular, Seidel (July 1996) teaches insemination deep into the uterine horn ipsilateral to the ovary. Seidel does not teach insemination both ipsi and contra-lateral within the uterine horns.

However, Seidel (1995) teaches ipsilateral and contra-lateral insemination of low dose semen into females. The reference teaches that pregnancy rates were nearly identical for ipsilateral and contra-lateral insemination.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (1996) so as to have performed the insemination procedure by inserting the semen both ipsi and contra-lateral into the uterine horns because this would have provided an equally effective means for inseminating female bovine.

8. Claims 205-207 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996) and Rens, and further in view of Seidel (Theriogenology (1994) 41: 168; cited in the IDS).

The teachings of Seidel (July and Jan 1996) and Rens are presented above. The combined references do not teach superovulating the females prior to insemination.

Seidel (1994) teaches methods for stimulating superovulation in cows. In the method of Seidel, cows are treated twice a day at 12 hour intervals with injections of 6, 6, 4, 4, 2, 2, 2, and 2 mg FSH and given three dosages of prostaglandin of 25 mg and 12.5 mg PGF-2-alpha on days 6 and 7, respectively, of FSH treatments. The

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superovulation treatment is initiated starting between days 9 and 14 of the estrous cycle.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to performed the surgical insemination procedure on females that were superovulated and synchronized using the FSH/PGF-2-alpha treatment methods as disclosed by Seidel (1994) in order to have achieved the benefit of providing a more effective and convenient means of insemination since the females could then be inseminated at the most optimal time during estrous and the timing of the insemination procedure could be scheduled to correspond with the collection and sorting of sperm.

9. Claim 203 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996) and Rens, as set forth above, and further in view of Rath (Theriogenology (1997) 47: 75-800; cited in the IDS) and Seidel (1995; cited in the IDS).

The teachings of Seidel (July and Jan 1996) and Rens are presented above. The combined references do not specify the solution into which the sperm cells are collected and thereby does not teach collecting the sorted sperm in a citrate solution containing about 6% egg yolk.

However, Rath (page 796) teaches collecting sex-sorted sperm into a collection media composed of TEST extender containing 2% hen egg yolk. Thus, Rath teaches the concept of collecting sperm sorted cells into a sperm extender medium.

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Additionally, Seidel (1995) teaches extending sperm in Cornell Universal Extender which is known to contain citrate and egg yolk.

In view of the teachings of Rath and Seidel (1995), it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (1996) so as to have collected the sperm in an extender comprising a citrate solution and egg yolk in order to have sorted the sperm into a medium that would help to preserve the sperm and/or which could be used for subsequently freezing of the sperm.

10. Claim 220 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996) and Rens, as set forth above, and further in view of Wilhelm (Cryobiology. 1996. 33: 320-329; cited in the IDS).

Seidel (July and Jan 1996) and Rens do not teach applying the artificial insemination method to equine sperm.

However, Wilhelm teaches the use of equine sperm for the purpose of artificial insemination. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the method of Rens to the sorting of equine sperm in order to have provided an effective means for distinguishing between and collecting populations of X- and Y-chromosome bearing sperm useful for artificially inseminating equine. Further, Wilhelm does not teach the quantity of equine used for artificial insemination. However, since the parameters which effect artificial insemination of equine were known in the art at the time the invention was made, it would have been obvious to one of ordinary skill in the art and well within the skill of the art to have

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selected an optimum quantity of sperm, wherein said quantity would be less than 25 million so as to have provided the most effective sample for inseminating equine while keeping the number of sperm to be used for insemination at the lowest possible number given the constraints on how many sperm could be sorted per day and the cost of sorting. Additionally, the ordinary artisan would have recognized that the quantity of sperm could be modified in order to have provided the most appropriate sperm sample depending on how the sample would be used – i.e., depending on the amount of sperm present in the original sample, whether the samples would be frozen prior to use, the number of samples to be used for insemination, and the type of insemination technique. Accordingly, to have generated sorted sperm samples containing less than 25 million sperm and to have used the sperm samples for artificial insemination of equine would have been obvious to one of ordinary skill in the art because the ordinary artisan would have recognized that the quantity of sperm could be and should be optimized to enhance the efficiency of the artificial insemination, while providing the most economical means for achieving artificial insemination.

11. Claims 200 and 201 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (July 1996) in view of Seidel (Jan 1996), Rens and Wilhelm, and further in view of Catt (Reprod. Dom. Animal (1997). 32: 251-258; cited in the IDS).

The teachings of Seidel, Rens, and Wilhelm are presented above.

Seidel (July 1996) does not teach establishing a sheath fluid which contains a HEPES buffered medium or sodium citrate.

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However, Catt teaches that semen may be diluted in a HEPES-buffered SOF (synthetic oviduct fluid) medium or a BTS solution containing sodium citrate and that such a fluids are suitable for maintaining the viability of spermatozoa (see, e.g., page 252 and 257). Catt also teaches that it is beneficial to sort into a medium containing a cushioning of seminal plasma to increase the viability and motility of sperm. Catt (page 256-257) teaches that while PBS is often used as a sheath fluid for sorting, it can be beneficial to include additional salts to the sheath fluid to increase the viability and motility of the sperm.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Seidel (July 1996) so as to have used a HEPES-buffered medium or a sodium citrate-containing medium for establishing a sheath fluid for sorting the sperm because Catt teaches that these solutions provide a suitable dilution medium for sperm and thereby using HEPES-buffered medium or a sodium-citrate containing solution as the sheath fluid would have achieved the benefit of ensuring the viability and motility of the sperm. Further, in the absence of evidence to the contrary, to have selected the optimum concentration of sodium-citrate, including 2.9%, based on the concentration and identity of other reagents in the sheath fluid would have been obvious to and well within the skill of the ordinary artisan at the time the invention was made.

Response to remarks regarding the previous 103 rejections:

In the response, Applicants traversed the previous grounds of rejection under 35 USC 103. Applicants state that Rens teaches only sample rates but does not teach sort

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rates. It is stated that less sperm are sorted each second than are analyzed and thereby the sample rates of Rens cannot be used to infer actual sort rates. This argument has been fully considered but is not persuasive. It is unclear as to how Applicants can assert that Rens does not teach sort rates equivalent to the claimed sort rates if Applicant believes that one cannot ascertain what sort rates were employed by Rens. Applicants' present specification appears to rely on the apparatus of Rens and similar apparatuses known in the prior art at the time the invention was made in order to achieve the separation of equine sperm at rates of at least 1200 sperm per second. Yet, it remains unclear as to why Applicants believe that they have achieved improved separation rates over Rens when they are unable to provide information regarding the separation rates of Rens.

It is noted that the present specification (page 25) provides only one example in which bovine sperm were sorted at rates of 500 sorts/second using a MoFlo® flow cytometer. The specification (page 11) states generally that rates of sorting "in the thousand and twelve hundred ranges have already been achieved through a high speed cell sorter." However, the specification does not provide any details regarding the high speed cell sorter that was used to achieve these results. Accordingly, the specification fails to disclose, and the claims fail to recite any particular steps, apparatus or other elements that are relied upon to provide improved sorting rates over those achieved using the modified MoFlo® apparatus equipped with the nozzle of Rens.

Applicants do not point to any particular limitations that are recited in the claims which distinguish the claims over the sorting method of Rens and which would thereby

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result in the asserted difference in technique and success rates. As set forth in the MPEP 716.02, the burden is placed on Applicant to establish that "the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992).

There must be a clear nexus between the asserted unexpected results and the method steps that allow for the unexpected results. Further, the claims must be commensurate in scope with the aspects of the invention which allow for the asserted unexpected results.

As discussed in the above rejection, Rens teaches that sampling rates of at least about 15,000 sorts/second can be used with the apparatus disclosed therein. In the absence of evidence to the contrary, it is maintained that such sampling rates would allow for sorting rates of 1200 sorts/second. Further, even if Rens does not specifically exemplify a method in which sort rates of 1200 sorts/sec are achieved, Rens provides the motivation to use the modified flow cytometer to achieve this sort rate because Rens specifically teaches the need to obtain large quantities of sorted sperm in a short period of time to allow for successful artificial insemination of mammals with sorted sperm (col. 4, lines 43-49; col. 5, lines 46-57).

No evidence has been provided by Applicants to indicate that the high speed flow sorter disclosed by Rens cannot be used to achieve sort rates of 1200 sorts/sec. Applicants are reminded that obviousness does not require absolute predictability but only the reasonable expectation of success. See In re Merck and Company Inc., 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986) and In re O'Farrell, 7 USPQ2d 1673 (Fed. Cir. 1988). Further, as stated in *Ex parte Kubin* (No. 2007-0819, Bd. Pat. App. & Int. May 31,

2007): "Under *KSR*, it is now apparent "obvious to try" may be an appropriate test in more situations than we previously contemplated. When there is motivation to solve a problem and there are a finite number of identified predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under 103. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct 1727, 82 USPQ2d 1385, 1397 (2007)." This reasoning is also applicable to the present situation wherein the prior art of Rens provides both the motivation to increase the rate of sorting and the means (i.e., the modified MoFlo® sorter equipped with the elliptical nozzle) to achieve the result of sorting at rates of 1200 sperm/sec.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 186-197, 199, 201-203, 205-208, 210-218 and 220 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as

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being unpatentable over claims 138-145 of U.S. Patent Application No. 09/744,675.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '675 are both drawn to methods for producing a nonhuman mammal wherein the methods comprise collecting sperm cells from a male, establishing a cell source which supplies sperm cells, sorting sperm cells so as to separate the sperm cells according to sex, inserting a portion of the sperm cells into a female and fertilizing at least one egg of said female. The present claims differ from the claims of '675 in that they are limited to methods for establishing an artificial insemination sample from any nonhuman mammal, whereas the methods of '675 are broadly drawn to methods for establishing an artificial insemination sample containing sperm cells from an equine. Since equine constitute a nonhuman mammal, the species set forth in the claims of '675 anticipates the claimed invention. Further, the present claims and the claims of '675 are both inclusive of methods in which high speed flow cytometry is used to separate sperm cells at a rate of at least 1200 sperm/s (i.e., greater than 900 sperm/s as recited in the claims of '675). The instant claims and the claims of '675 also are inclusive of methods in which the sheath fluid contains a HEPES buffered medium, methods in which a low dose of sperm cells is utilized and methods in which fertilization success rates of from 35% to 90% of that of a typical unsorted insemination dosage are achieved.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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13. Claims 186-197, 199-200, 2022, 203, 205-208 and 210-219 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 124-141 of U.S. Patent Application No. 10/081,955. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '955 are both drawn to methods for producing a nonhuman mammal wherein the methods comprise collecting sperm cells from a male, establishing a cell source which supplies sperm cells, sorting sperm cells rates of at least 1200 sorts/second (e.g., rates of greater than 500 or 2000 sorts/sec, claims 137 and 138 of '955) so as to separate the sperm cells according to sex, inserting a portion of the sperm cells into a female and fertilizing at least one egg of said female. The instant claims and the claims of '955 also are inclusive of methods in which the sheath fluid contains a HEPES buffered medium, methods in which a low dose of sperm cells is utilized, methods in estrus is synchronized, methods in which a sheath fluid containing 2.9% sodium citrate is utilized and methods in which the collection container has a wide opening. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 186-189, 191-197, 199, 202, 210-213, 215, and 217-219 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7195920 (cited in the IDS of July 2007) in view of Seidel (July 1996). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '920 are both inclusive of methods comprising establishing a cell source, establishing a

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sheath fluid environment, sensing a property of viable sperm cells, discriminating between sperm cells based on a sex characteristic at a rate of at least about 1200 sorts per second, and collecting sorter sperm cells having the desired sex characteristics by collecting the sperm cells in a container in which the cells are cushioned from impact with the container. The claims of '920 do not recite the additional steps of freezing the sorted sperm cells, thawing the sorted sperm cells, performing artificial insemination of a female non-human mammal with the sorted sperm cells and fertilizing at least one egg of the female non-human mammal. However, Seidel teaches that sperm can be frozen and then thawed and extremely low numbers of the sperm can be used for artificial insemination. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method claimed in '920 so as to have frozen and then thawed the frozen sperm and to have used low numbers of the sperm for artificial insemination in order to have provided an effective means for storing and transporting the sex-sorted sperm for subsequent use in artificial insemination.

Regarding claims 191-194, Seidel (July 1996) teaches inserting the semen deep into each uterine horn using an embryo transfer gun (i.e., "embryo transfer equipment").

Regarding claim 195, Seidel (July 1996) teaches performing the artificial insemination procedure 12 hours after the onset of estrous. Regarding claims 196 and 197, Seidel (July 1996) does not teach using the artificial insemination sample within 17 or 10 hours of establishing the sample. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the artificial insemination sample as soon as possible following the formation of the sample in order to have

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ensured the viability of the sample, thereby improving the overall effectiveness of the insemination procedure. Regarding claim 217-219, Seidel teaches using 2 or 5×10^5 total sperm. This is considered to be about one half or less than about 10% of sperm cells are used for insemination relative to an unstated amount of a "typical insemination sample."

15. Claim 190 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7195920 in view of Seidel (July 1996) and further in view of Seidel (1995). The claims of '920 do not recite performing insemination both ipsi and contra-lateral within the uterine horns.

However, Seidel (1995) teaches ipsilateral and contra-lateral insemination of low dose semen into females. The reference teaches that pregnancy rates were nearly identical for ipsilateral and contra-lateral insemination. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of claims '920 and Seidel (1996) so as to have performed the insemination procedure by inserting the semen both ipsi and contra-lateral into the uterine horns because this would have provided an equally effective means for inseminating female bovine.

16. Claims 208, 214 and 216 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7195920 in view of Seidel (July 1996) and further in view of Rens. The claims of '920 do not recite staining the sperm cells with a solution of 38uM stain and then concentrating the sperm. However, Rens (col. 5) teaches staining the sperm with

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7.1 uM Hoechst 3342 dye per 15×10^6 sperm for 40 min at 32C, sorting the sperm cells and then concentrating the sperm cells. It is noted that the present claims do not specify the type of stain, the final concentration of stain, the number of sperm or the conditions for staining the sperm. However, at the time the invention was made the parameters which effect staining of sperm cells prior to sorting were well known in the art. Thereby, to have determined the optimum concentration of stain, depending on the quantity of sperm and the conditions (time, temp) of staining would have been obvious to one of ordinary skill in the art and well within the skill of the art. As discussed in MPEP 2144.05(b), "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)." Accordingly, it would have been obvious to one of ordinary skill in the art and well within the skill of the art to have selected the optimum concentration of stain depending on the concentration of sperm, and the conditions of staining, including to have selected the concentration of 38 uM content of stain, in order to have provided the most effective means for staining the sperm to allow for accurate sorting, while maintaining the integrity and viability of the sperm. Further, with respect to claim 216, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have established a collection container having stream matched physical characteristics in order to have provided the benefit of preserving the integrity

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of the sperm cells. Regarding claims 214, the claims of '920 do not specify the size of the collection container. However, it would have been well within the skill of the art at the time the invention was made to have selected a collection container of an appropriate width in order to have prevented damaging the sperm since Rens teaches the criticality of the dimensions of the sorting device and the orientation of the sperm within the sorting device in order to maintain sperm viability (see, for example, column 3).

17. Claim 220 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7195920 in view of Seidel (July 1996) and Wilhelm. The teachings of the claims of '920 and Seidel are presented above. The claims of '920 recite a method of sorting sperm from any organism, but do not specifically teach sorting equine sperm. However, Wilhelm teaches the use of equine sperm for the purpose of artificial insemination. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the sorting method claimed in '920 to the sorting of equine sperm in order to have provided an effective means for distinguishing between and collecting populations of X- and Y-chromosome bearing sperm useful for artificially inseminating equine. Further, Wilhelm does not teach the quantity of equine used for artificial insemination. However, since the parameters which effect artificial insemination of equine were known in the art at the time the invention was made, it would have been obvious to one of ordinary skill in the art and well within the skill of the art to have selected an optimum quantity of sperm, wherein said quantity would be less than 25 million so as to have

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provided the most effective sample for inseminating equine while keeping the number of sperm to be used for insemination at the lowest possible number given the constraints on how many sperm could be sorted per day and the cost of sorting. Additionally, the ordinary artisan would have recognized that the quantity of sperm could be modified in order to have provided the most appropriate sperm sample depending on how the sample would be used – i.e., depending on the amount of sperm present in the original sample, whether the samples would be frozen prior to use, the number of samples to be used for insemination, and the type of insemination technique. Accordingly, to have generated sorted sperm samples containing less than 25 million sperm and to have used the sperm samples for artificial insemination of equine would have been obvious to one of ordinary skill in the art because the ordinary artisan would have recognized that the quantity of sperm could be and should be optimized to enhance the efficiency of the artificial insemination, while providing the most economical means for achieving artificial insemination.

18. Claims 200 and 201 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7195920 in view of Seidel (July 1996) and Wilhelm and further in view of Catt . The teachings of the claims of '920, Seidel and Wilhelm are presented above. The claims of '920 do not sorting equine or bovine sperm using a sheath fluid which contains a HEPES buffered medium or sodium citrate. However, Catt teaches that semen may be diluted in a HEPES-buffered SOF (synthetic oviduct fluid) medium or a BTS solution containing sodium citrate and that such a fluids are suitable for maintaining the viability

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of spermatozoa (see, e.g., page 252 and 257). Catt also teaches that it is beneficial to sort into a medium containing a cushioning of seminal plasma to increase the viability and motility of sperm. Catt (page 256-257) teaches that while PBS is often used as a sheath fluid for sorting, it can be beneficial to include additional salts to the sheath fluid to increase the viability and motility of the sperm. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Seidel (July 1996) so as to have used a HEPES-buffered medium or a sodium citrate-containing medium for establishing a sheath fluid for sorting the sperm because Catt teaches that these solutions provide a suitable dilution medium for sperm and thereby using HEPES-buffered medium or a sodium-citrate containing solution as the sheath fluid would have achieved the benefit of ensuring the viability and motility of the sperm. Further, in the absence of evidence to the contrary, to have selected the optimum concentration of sodium-citrate, including 2.9%, based on the concentration and identity of other reagents in the sheath fluid would have been obvious to and well within the skill of the ordinary artisan at the time the invention was made.

19. Claim 203 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7195920 in view of Seidel (July 1996) and further in view of Rath (Theriogenology (1997) 47: 75-800; cited in the IDS) and Seidel (1995; cited in the IDS). The claims of '920 do not recite collecting the sorted sperm in a citrate solution containing about 6% egg yolk.

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However, Rath (page 796) teaches collecting sex-sorted sperm into a collection media composed of TEST extender containing 2% hen egg yolk. Thus, Rath teaches the concept of collecting sperm sorted cells into a sperm extender medium. Additionally, Seidel (1995) teaches extending sperm in Cornell Universal Extender which is known to contain citrate and egg yolk. In view of the teachings of Rath and Seidel (1995), it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (1996) so as to have collected the sperm in an extender comprising a citrate solution and egg yolk in order to have sorted the sperm into a medium that would help to preserve the sperm and/or which could be used for subsequently freezing of the sperm.

20. Claims 205-207 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No.

7195920 in view of Seidel (July 1996) and further in view of Seidel (Theriogenology (1994) 41: 168; cited in the IDS). The claims of '920 do not recite superovulating the female non-human bovine prior to insemination. However, Seidel (1994) teaches methods for stimulating superovulation in cows. In the method of Seidel, cows are treated twice a day at 12 hour intervals with injections of 6, 6, 4, 4, 2, 2, 2, and 2 mg FSH and given three dosages of prostaglandin of 25 mg and 12.5 mg PGF-2-alpha on days 6 and 7, respectively, of FSH treatments. The superovulation treatment is initiated starting between days 9 and 14 of the estrous cycle.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to performed the

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surgical insemination procedure on females that were superovulated and synchronized using the FSH/PGF-2-alpha treatment methods as disclosed by Seidel (1994) in order to have achieved the benefit of providing a more effective and convenient means of insemination since the females could then be inseminated at the most optimal time during estrous and the timing of the insemination procedure could be scheduled to correspond with the collection and sorting of sperm.

Response to remarks regarding the obvious-type double patenting rejections:

In the response to the previous obviousness-type double patenting rejections, Applicants suggest that the amendments to the claims may have obviated the rejections. However, the amendments to the claims do not overcome the obviousness-type double patenting rejections and these rejections are maintained for the reasons stated above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Carla Myers/

Primary Examiner, Art Unit 1634